

**Amendments To The Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

22. (Presently amended) A method for producing a preparation for transporting at least one active ingredient through the skin or mucous membrane of a mammal comprising:

a. selecting a first amphiphilic lipid component; and  
b. selecting a second amphiphilic lipid component and selecting at least one active ingredient; **[[or**

c. selecting an amphiphilic active ingredient to form a second amphiphilic lipid component, and optionally selecting one or more further active ingredients;]]

**[[d]]** c. said first and second amphiphilic lipid components being selected so that the solubility of the second amphiphilic lipid component in a pharmaceutically acceptable suspending medium is at least ten times greater than the solubility of the first amphiphilic lipid component in said medium;

**[[e]]** d. adapting the composition or concentration of the preparation for transport through skin or mucous membrane, by adjusting the content of the more soluble component to less than 0.1 mole percent of **[[the content of the first and second amphiphilic lipid components]]** its content at which the enveloped droplets **[[stabilize]]** solubilize, if there is a solubilizing point; and

**[[f]]** e. adjusting the content of amphiphilic lipid components, such that the ratio of the permeation capability relative to reference particles which are much smaller than the constrictions of the barrier, wherein the reference particles are water molecules, is between 10<sup>-5</sup> and 1;

**[[g]]** f. producing a transfersome suspension by means of applying energy to the mixture of said amphiphilic lipid components including at least one active ingredient, said transfersomes comprising liquid droplets encompassed within a sheath comprising said amphiphilic lipid components, said amphiphilic lipid components being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized, said active ingredient being contained in said liquid droplets, or in said sheath, or in both said liquid droplets and said sheath.

23. (Original) The method of claim 22, characterized in that the content of amphiphilic components is adjusted, so that the ratio of the permeation capability relative to reference particles, which are much smaller than the constrictions in the barrier, for example water, when the barrier itself is the site of determination, is between  $10^{-5}$  and 1, preferably between  $10^{-4}$  and 1 and especially between  $10^{-2}$  and 1.

24. (Previously presented) The method of claim 22 wherein stability and permeation capability are determined by filtration under pressure through a filter having pore size ranging from about 30 to about 100 nm or by controlled mechanical whirling up, shearing or comminuting.

25. (Previously presented) The method of claim 22, wherein the stability and permeation capability is determined by mechanical comminuting effects.

26. (Previously presented) The method of claim 22 wherein the transfersome preparation is produced from at least to amphiphilic components of different polarity, at least one polar pharmaceutically acceptable medium and at least one active ingredient.

27. (Previously presented) The method of claim 22, wherein said amphiphilic component(s) comprises or contains the active ingredient, and said transfersomes are formed from at least two amphiphilic components of different polarity and at least one polar pharmaceutically acceptable medium.

28. (Previously presented) The method of claim 22 wherein said amphiphilic components and a hydrophilic substance are mixed separately with an active ingredient and optionally brought into solution and then combined to form transfersomes by supplying mechanical energy.

29. (Previously presented) The method of claim 22 wherein said amphiphilic components, either as such or dissolved in a physiologically compatible solvent or

solutizer, which is miscible with a polar liquid or liquids, are combined with a polar pharmaceutically acceptable medium.

30. (Previously presented) The method of claim 22, wherein said transfersomes are formed by a method selected from the group consisting of stirring; evaporation from a reverse phase; an injection method; a dialysis method; electrical stressing; thermal stressing; a mechanical stressing selected from the group consisting of shaking, stirring, homogenizing, ultrasonication, rubbing, freezing, thawing, heating and cooling; and high pressure filtration and low pressure filtration.

31. (Previously presented) The method of claim 22, wherein the formation of the transfersomes is brought about by filtration and the filter material used in said filtration has a pore size of 0.01 to 0.8  $\mu\text{m}$ .

32. (Previously presented) The method of claim 22, wherein the association between carrier and active ingredients takes place at least partially after the droplet formation.

33. (Presently amended) The method of claim 22, wherein shortly before use, the enveloped droplets are prepared from a concentrate or lyophilisate, which was prepared from said transfersome suspension.

49. (Presently amended) The method of claim 23, wherein the permeation relative to water is between  $10^{-4}$  and 1.

50. (Presently amended) The method of claim 23, wherein the permeation relative to water is between  $10^{-2}$  and 1.

51. (Presently amended) The method of claim 31, wherein the filter material has a pore size of 0.05 to 0.3  $\mu\text{m}$ .

52. (Presently amended) The method of claim 31, wherein the formation of the filter material has a pore size of 0.08 to 0.15  $\mu\text{m}$ .

53. (Previously presented) A method of treatment of a mammal in need thereof, the method comprising administering to the skin or mucous membrane of the mammal a preparation for the transport of at least one active agent through the skin or mucous membrane of the mammal, the preparation comprising:

transfersomes suspended in a pharmaceutically acceptable medium for application onto the skin or mucous membrane of a mammal, said transfersomes comprising:

liquid droplets encompassed within a sheath, said sheath comprising:

a first amphiphilic lipid component, a second amphiphilic lipid component and at least one active agent, or

a first amphiphilic lipid component, a second amphiphilic lipid component comprising an amphiphilic active agent and, optionally, one or more further active agents,

wherein said first and second amphiphilic lipid components differ in their solubility in said pharmaceutically acceptable medium by a factor of at least 10, said first and second amphiphilic lipid components being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized, said active agent(s) being contained in said liquid droplets, or in said sheath, or in both said liquid droplets and said sheath, or being identical to the more soluble amphiphilic lipid component .

54. (Previously presented) The method of claim 53, wherein the solubility of the more soluble component(s) is at least  $10^{-3}$  M to  $10^{-6}$  M and the solubility of the less soluble component is at least  $10^{-6}$  M to  $10^{-10}$  M.

55. (Previously presented) The method of claim 53, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between  $10^0$  M and  $10^7$  M.

56. (Previously presented) The method of claim 55, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between  $10^2$  M and  $10^6$  M.

57. (Previously presented) The method of claim 55, wherein the difference between the solubility of the more soluble component(s) and the less soluble component(s) is approximately between  $10^3$  M and  $10^5$  M.

58. (Previously presented) The method of claim 53, wherein the preparation permeating through said skin or mucous membrane has a permeability of at least 0.001% of the permeability of small molecules, which permeate essentially without being impeded.

59. (Previously presented) The method of claim 53, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-5}$  M and 1 M.

60. (Previously presented) The method of claim 59, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-4}$  M and 1 M.

61. (Previously presented) The method of claim 59, wherein the permeation capability relative to reference particles  $P_{(\text{transfer.})}/P_{(\text{refer.})}$ , the reference particles being water, is between  $10^{-2}$  M and 1 M.

62. (Previously presented) The method of claim 53, wherein the content of said at least one active agent in the preparation does not change significantly during transport through the skin or mucous membrane.

63. (Previously presented) The method of claim 62, wherein the sheath is a double layer.

64. (Previously presented) The method of claim 53, wherein the vesicle radius of the transfersome is between about 25 nm to about 500 nm.
65. (Previously presented) The method of claim 64, wherein the vesicle radius is between about 80 nm and about 100 nm.
66. (Previously presented) The method of claim 64, wherein the vesicle radius is between about 80 nm and about 100 nm.
67. (Previously presented) The method of claim 53, wherein said amphiphilic components comprise lipids of different polarity.
68. (Previously presented) The method of claim 67, wherein the less polar amphiphilic lipid component is a phospholipid, and a second, more soluble amphiphilic component is an active ingredient, the concentration of the more soluble component(s) being between 0.01% by weight and 15% by weight.
69. (Previously presented) The method of claim 68, wherein the concentration of the more soluble component(s) is between 0.1% by weight and 10% by weight.
70. (Previously presented) The method of claim 68, wherein the concentration of the more soluble component(s) is between 0.1% by weight and 3% by weight.
71. (Previously presented) The method of claim 68, wherein the total lipid concentration being between about 0.5% by weight and 15% by weight.
72. (Previously presented) The method of claim 68, wherein the total lipid concentration being between about 1% by weight and 10% by weight.
73. (Previously presented) The method of claim 68, wherein at least one amphiphilic lipid component is selected from the group consisting of a diacyl or a dialkyl glycerophosphoethanolamino azo polyoxyethylene derivative, a didecanoyl

phosphatidyl choline, a diacyl phosphooligomaltobionamide, a glyceride, a glycerophospholipid, a isoprenoid lipid, a sphingolipid, a steroid, a half protonated liquid fatty acid, a phosphatidyl choline, a phosphatidyl ethanolamine, a phosphatidyl glycerol, a phosphatidyl inositol, a phosphatid acid, a phosphatidyl serine, a sphingomyelin, a sphingophospholipid, a glycosphingolipid, a cerebroside, a ceramide polyhexoside, a sulfatide, a sphingoplasmalogen, a ganglioside, and a glycolipid.

74. (Previously presented) The method of claim 53, wherein at least one amphiphilic component is a synthetic lipid.

75. (Previously presented) The method of claim 53, wherein at least one amphiphilic lipid component is selected from the group consisting of a sulfur containing lipid and a hydrocarbon-containing lipid which forms stable structures.

76. (Previously presented) The method of claim 53, wherein at least one amphiphilic lipid component is an identical

77. (Previously presented) The method of claim 75, wherein the stable structures are double layers.

78. (Previously presented) The method of claim 53, wherein at least one amphiphilic lipid component is selected from the group consisting of dioleoyl phospholipid, a dilinoyl phospholipid, a dilinolenyl phospholipid, a dilinoyl phospholipid, a dilinolinoyl phospholipid, a diarachinoyl phospholipid, a dilauroyl phospholipid, a dimyristoyl phospholipid, a dilalmitoyl phospholipid, a distearoyl phospholipid, and corresponding dialkyl or sphingosin derivatives thereof.

79. (Previously presented) The method of claim 53, wherein at least glycosphingolipid is selected from the group consisting of cerebroside, ceramide polyhexoside, sulfatide and sphingoplasmaologen.

80. (Previously presented) The method of claim 53, wherein the less soluble amphiphilic lipid component is selected from the group consisting of a myristoleoyl, a

palmitoleoyl, a petroselinyl, a petroselaidyl, a oleoyl, elaidyl, a cis- or trans- vaccenoyl, a linolyl, a linolenyl, a linolaidyl, a octadecatetraenoyl, a gondoyl, a eicosaenoyl, a eicosadienoyl, a eicosatrienoyl, a arachidoyl, a cis- or trans-docosaenoyl, a docosadienoyl, a docosatrienoyl, a docosatetraenoyl, a caproyl, a lauroyl, a tridecanoyl, a myristoyl, a pentadecanoyl, a palmitoyl, a heptadecanoyl, a stearoyl or a nonadecanoyl, a glycerol-phospholipid, a glycolipid, an acyl lipid, and an alkyl lipid.

81. (Previously presented) The method of claim 53, wherein the total content of the amphiphilic component is between 0.01 and 40% by weight of the preparation.

82. (Previously presented) The method of claim 75, wherein the total content of the amphiphilic component is between about 0.1 and 15% by weight.

83. (Previously presented) The method of claim 75, wherein the total content of the amphiphilic component is between about 1 and 10% by weight.

84. (Previously presented) The method of claim 53, wherein the active agent is selected from the group consisting of an adrenocorticostatic agent, a  $\beta$ -adrenolytic agent, an androgen, and antiandrogen, an anti-parasitic, an anabolic, an anesthetic, an non-narcotic analgesic, an analeptic, an anti-allergic, an anti-arrhythmic, an anti-arteriosclerosis, an anti-asthmatic, a bronchospasmolytic agent, an antibiotic, an anti-depressive agent, an anti-psychotic agent, and anti-diabetic agent, an antidote, an anti-emetic, and anti-epileptic, an anti-fibrinolytic, and anti-convulsive agent, an anti-cholinergic agent, an enzyme, a coenzyme, a coenzyme inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anto-mycotic, an antimyasthenic agent, an active ingredient against Parkinson's disease, an active ingredient against Alzheimer's disease, an anti-phlogistic, an anti-pyretic, an anti-rheumatic agent, an antiseptic, a respiratory analeptic, a respiratory stimulating agent, a broncholytic, a cardiotonic agent, a chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucocorticoid, a therapeutic agent for influenza, a hemostatic agent, a hypnotic agent, an immunoglobulin, a bioactive carbohydrate, a contraceptive, a



migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural therapeutic agent, a CNS therapeutic agent, a nucleotide, a polynucleotide, a neuroleptic agent, a neuron transmitter, a neuron transmitter antagonist, a peptide, a peptide derivative, a ophthalmic agent, a para-sympathicomimetic or para-sympathicolytic agent, a protein, a protein derivative, a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, a rhinological agent, a soporific, a soporific antagonist, a sedative, a spasmolytic, a tuberculosis agent, a urological agent, a vasoconstrictor, a vasodilator, a virostatic agent, a wound-healing agent, and a non-steroidal antiinflammatory agent.

85. (Previously presented) The method of claim 53, wherein the active agent is a nonsteroidal anti-inflammatory drug selected from the group consisting of diclofenac, ibuprofen, and a lithium, sodium, potassium, cesium, rubidium, ammonium, monoethyl, dimethyl, trimethylammonium or ethylammonium salt thereof.

86. (Previously presented) The method of claim 53, wherein the preparation comprises consistency modifiers selected from the group consisting of a hydrogel, an antioxidant selected from the group consisting of a probucol, a tocopherol, a BHT, an ascorbic acid, a desferroxamine or a stabilizer selected from the group consisting of a phenol, a cresol, and a benzyl alcohol.

87. (Previously presented) The method of claim 53, wherein the active agent is a growth regulating substance.

88. (Previously presented) The method of claim 53, wherein the active agent is selected from the group consisting of an insecticide, a pesticide, a herbicide or a fungicide.

89. (Previously presented) The method of claim 53, wherein the active agent is an allurement.

90. (Previously presented) The method of claim 53, further comprising one or more solubilizing components in an amount effective to provide adequate deformability to

said transfersomes, such that said transfersomes are capable of passing through said skin or mucous membrane without being solubilized, the amount of solubilizing components included in said preparation being less than 0.1 mole percent at which the solubilizing point of the enveloped droplets is reached, based on the content of said amphiphilic lipid components.

91. (Previously presented) The method of claim 90, wherein the ratio of the permeation capability relative to reference particles which are much smaller than the constrictions of the test barrier is between  $10^{-2}$  and 1.

92. (Previously presented) The method of claim 22, wherein the transfersomes are produced by a method selected from the group consisting of filtration, treatment with ultrasound, stirring and shaking